

**REMARKS**

Entry of the foregoing, reexamination and further and favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested.

The Office Action Summary correctly indicates that claims 1-12 are pending in the application. Claims 1-12 are under consideration and stand rejected.

Claims 1 and 2 have been amended for consistency in the use of terms. Support for the claims as amended is implicit in the claims as originally filed.

The Sequence Listing has been amended for better consistency of the description of SEQ ID NOS: 5 and 6 therein with the descriptions of these sequences in the Specification.

No prohibited new matter has been introduced by way of the above amendments. Applicants reserve the right to file a continuation or divisional application on subject matter canceled by way of this Amendment.

***Claim rejections-35 USC§112***

Claim 1 has been rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter with application regards as the invention. The Examiner asserted that the claim contained both a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation. More specifically, the Examiner indicated that claim 1 contained the broad recitation "comprising about 19 contiguous nucleotides" as well as "capable of forming a double stranded RNA of about 19 to 200 nucleotides in length."

Applicants respectfully traverse. The two recitations of lengths do not refer to the same property. The first recitation of "at least 19 nucleotides" defines a minimum length for either sense or antisense to the nucleotide sequence of the gene of interest, whereas the second recitation refers to the length of the region of double stranded RNA formed by the basepairing between the sense and antisense nucleotide sequence which should range between about 19 to about 200 basepairs. However, sense and antisense strands may be of differing lengths and need not be complementary along their entire lengths, but only in a region of about 19 to about 200 basepairs.

Without acquiescing to the Examiner's rejection, and solely to expedite prosecution, the claims have been amended. Applicants respectfully submit that the metes and bound of

the claims as amended would be understood by a person of ordinary skill in the art. Accordingly, Applicants respectfully request withdrawal of the rejection.

***Claim rejections-35 USC§103***

Claims 1-12 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Wesley et al. The Plant Journal, 2001 Vol. 27, No. 6: pp 581-590 in view of Yukawa et al. Plant Molecular Biology, 2002,; vol. 50, pp 713-723 and Applicants' specification.

The prior art fails to establish a proper *prima facie* case of obviousness. To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. M.P.E.P. § 2143.

The Office has not met its burden in making the rejection, because the prior art fails to establish a proper *prima facie* case of obviousness. To establish a *prima facie* case of obviousness, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. M.P.E.P. § 2143; *In re Rouffet*, 47 U.S.P.Q.2d 1453, 1458 (Fed. Cir. 1998) ("[T]he suggestion to combine requirement stands as a critical safeguard against hindsight analysis and rote application of the legal test for obviousness.") Rejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness. *KSR Int'l Co. v. Teleflex Inc.*, \_\_\_ U.S. \_\_\_, 127 S.Ct. 1727, 1739, 82 U.S.P.Q.2d 1385, 1396 (April 30, 2007) (citing *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329 (Fed. Cir. 2006)).

The Examiner has alleged that it would have been obvious at the time of the invention to modify the disclosure of Wesley et al. teaching post transcriptional silencing of plant genes using ihpRNA as small as 98 base pairs by replacing the promoter for a PolIII type 3 promoter in view of the disclosure by Yukawa, which according to the Examiner teaches the use of 7SL type 3 PolIII promoter and POLIII type 3 promoters in general in plant cells for driving gene inhibition in plants.

In as far as the rejection still applies to the amended claims, the rejection is respectfully traversed. Whereas Applicants agree that Wesley et al. does not teach or suggest the use of a Pol III-type 3 promoter, Applicants submit that Yukawa et al. does not cure this defect in Wesley et al as the Examiner has alleged..

The Examiner has alleged that Yukawa et al. teaches use of Pol III promoters expressing in transformed plants and plant cells. OFFICE ACTION at 5, line 4 from the bottom. However, as indicated in the title of that publication, the teaching of Yukawa et al. is limited to demonstrating that plant 7SL RNA genes with inserted antisense or ribozyme sequences are transcribed in an in vitro transcription system, in a homologous plant extract. *See also* Yukawa et al. at abstract line 7, or page 719, 2<sup>nd</sup> column lines 19-20.

Yukawa et al. does not teach or even suggest any use of such chimeric genes in in vivo plant cells. Yukawa is entirely silent about the gene silencing effect that may or may not be obtained with the described constructs in transformed plant cells. The authors themselves conclude only that the currently reported experiments are a *"first report of demonstrating the employment of 7SL RNA genes as potential cassettes for the expression of antisense RN"* Yukawa at Abstract, last sentence (emphasis added). Yukawa does not teach that they demonstrate success in using Pol III promoters for driving gene inhibition in plants.

Clearly, in view of the absence of any teaching with regard to gene silencing in plant cells or plants, there is no incentive or motivation for the skilled artisan to replace the promoter in the constructs disclosed by Wesley et al. for the promoters taught by Yukawa et al. to be capable of transcription of antisense or ribozyme constructs in *in vitro* cell extracts.

Furthermore, the present inventors discovered and the current specification teaches that the use of Pol III type 3 promoter driven hairpin RNA gene silencing is unexpectedly more effective than Pol II promoter (CaMV35S) driven hairpin RNA gene silencing for short double stranded RNA molecules. This is demonstrated at least in Example 2, page 24, lines 6-10; Example 3, paragraph spanning pages 25 and 26; Example 5, page 29, first sentence. Example 6, page 31, first sentence.

The underlying discovery, summarized in the tabulated results of the specification Examples, demonstrates that gene silencing effected by short hpRNA is more effective, both for transgenes and endogenous genes, when such short hpRNAs are generated from chimeric genes comprising a Pol III type 3 promoter rather than from chimeric genes comprising a Pol II promoter.

The combination of Wesley et al. nor Yukawa et al. do not provide any motivation or suggestion to make the claimed invention. Neither Wesley et al. nor Yukawa et al. appreciated and do not teach or suggest that use of a Pol III type 3 promoter to generate a short double stranded RNA molecule would lead to more effective gene silencing than the use of a Pol II promoter.

Accordingly, Applicants submit that it would not have been obvious at the time of the invention to replace the POLII promoter used by Wesley et al. for the Pol III promoter used in an in vitro nuclear extract by Yukawa et al. to arrive at the currently claimed invention with a reasonable expectation of success in view of the absence of any teaching that Pol III promoters would be useful in transformed plant cells for driving gene inhibition, let alone that they would lead to hpRNA mediated gene silencing with enhanced efficiency compared to Pol II promoter driven transgenes.

A specific understanding or principle within the knowledge of a skilled artisan that would have motivated one to make the combination in the manner claimed is required to make out a proper *prima facie* case of obviousness. *In re Kotzab*, 55 U.S.P.Q.2d 1313, 1318 (Fed. Cir. 2000). In other words, the Examiner must provide a logical reason as disclosed in the prior art at the time of the invention for combining the references so as to arrive at the invention. Otherwise, the use of such teachings as evidence of obviousness must be considered impermissible hindsight. *Ex parte Stauber*, 208 U.S.P.Q. 945, 946 (Bd. App. 1980). The Office has relied upon merely conclusory statements regarding the motivation and expectation of success allegedly provided by the asserted combination. These statements are not sufficient to meet the Office's burden of presenting a logical reason for the rejection that is supported by sound scientific evidence in the prior art.

**CONCLUSION**

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned concerning such questions so that prosecution of this application may be expedited.

The Director is hereby authorized to charge any appropriate fees that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800.

Respectfully submitted,

BUCHANAN INGERSOLL PC

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